UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,529	11/12/2007	Wilhelmus Everhardus Hennink	313632002700	9955

25225 7590 01/12/2011

MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
DICKINSON, PAUL W	
ART UNIT	**PAPER NUMBER**
1618	

NOTIFICATION DATE	DELIVERY MODE
01/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

EOfficeSD@mofo.com

Office Action Summary	Application No.	Applicant(s)	
	10/593,529	HENNINK ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/13/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7 and 10-16 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/09198 (WO '198; document already in record). WO '198 discloses a temperature sensitive polymer having a lower critical solution temperature that changes during incubation in an aqueous solution or medium, which polymer is a hydroxylpropyl methacrylamide (oligo)lactate (abstract; page 8, line 24 to page 10, line 7; examples; claims 1-20). Such a polymer is a homo polymer of a hydrophobically modified hydroxyalkyl(meth)acrylamide wherein the hydrophobic group ((oligo)lactate) is bound through a hydrolysable bond. This satisfies instant claims 1-7 and 10. Since the polymers change the LCST during incubation (abstract; page 15, lines 10-14), they are used as controlled release systems and targeting drug compositions, the targeting drug composition may further comprise a homing device (claim 12), which satisfies instant claims 11 and 15-16. The controlled release system may be in the form of a polymeric

micelle in which polyethylene glycol is a hydrophilic block (claim 10), which satisfies instant claim 12. The polymer may be a hydrogel with an ABA block structure (claim 18), which satisfies instant claims 13-14.

Claims 1-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Cadée et al (Cadée et al, Synthesis, characterization of 2-(methacryloyloxy)ethyl-(di-L-lactate and their application in dextran-based hydrogels, *Polymer*, 40, 1999, 6877-6881). Cadée discloses N-(2-hydroxypropyl)methacrylamide dilactate coupled to dextran and formed into a hydrogel (page 6879, section 2.6). Such a polymer is a homo polymer of a hydrophobically modified hydroxyalkyl(meth)acrylamide wherein the hydrophobic group (di-lactate) is bound through a hydrolysable bond. This satisfies instant claims 1-7 and 10.

Regarding instant claim 10, although Cadée does not appreciate that the N-(2-hydroxypropyl)methacrylamide dilactate coupled to dextran hydrogel has a lower critical solution temperature before incubation below human body temperature and a different lower critical solution temperature after incubation above human body temperature, the composition must inherently have this property because it meets all the structural limitations of instant claim 10, i.e. a temperature sensitive polymer which polymer is a homo polymer of a hydrophobically modified hydroxyalkyl(meth)acrylamide. As a composition cannot be separated from its properties, the composition of Cadée must inherently provide the instantly disclosed properties, i.e. the properties of claim 10. "'[T]he discovery of a previously unappreciated property of a prior art composition, or of

a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.' Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)." MPEP § 2112, I.

Claims 1-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by van Dijk-Wolthuls et al (van Dijk-Wolthuls et al, A new class of polymerizable dextrans with hydrolysable groups: hydroxyethyl methacrylated dextran with and without oligolactate spacer, *Polymer*, 38, 1997, 6235-6242). Van Dijk Wolthuls et al discloses N-(2-hydroxypropyl)methacrylamide olig(lactates) coupled to dextran and formed into a hydrogel (Experimental section). Such a polymer is a homo polymer of a hydrophobically modified hydroxyalkyl(meth)acrylamide wherein the hydrophobic group ((oligo)lactate) is bound through a hydrolysable bond. This satisfies instant claims 1-7 and 10.

Regarding instant claim 8, the polymer is made by adding varying ratios of L-lactide to HEMA and the reference teaches that the length of the lactide spacer can be controlled by adjusting the lactide/HEMA ratio and reaction time (pages 6238-6239, *Synthesis of HEMA-lactate*). The polymers made used varying ratios of L-lactide to HEMA which in one embodiment led to 2 and 4 lactyl residues per HEMA (page 6238, col 2). This corresponds to Applicant's copolymer of instant claim 8, where the HEMA

units having 4 lactyl units corresponds to instant claim 8 monomer unit (a) and the HEMA units having 2 lactyl corresponds to instant claim 8 monomer unit (b).

Regarding instant claim 10, although van Dijk-Wolthuls et al does not appreciate that the N-(2-hydroxypropyl)methacrylamide dilactate coupled to dextran hydrogel has a lower critical solution temperature before incubation below human body temperature and a different lower critical solution temperature after incubation above human body temperature, the composition must inherently have this property because it meets all the structural limitations of instant claim 10, i.e. a temperature sensitive polymer which polymer is a homo polymer of a hydrophobically modified hydroxyalkyl(meth)acrylamide. As a composition cannot be separated from its properties, the composition of Cadée must inherently provide the instantly disclosed properties, i.e. the properties of claim 10. "'[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.' Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)." MPEP § 2112, I.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 10-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neradovic et al (Neradovic et al, Thermoresponsive Polymeric Micelles with Controlled Instability Based on Hydrolytically Sensitive N-Isopropylacrylamide Copolymers, *Macromolecules*, 34, 2001, 7589 – 7591). Neradovic discloses a NIPPAAm/ N-(2-hydroxypropyl)methacrylamide lactate copolymer and micelles made from AB block copolymer containing a PEG block and a NIPPAAm/ N-(2-hydroxypropyl)methacrylamide lactate block (page 7590, tables). The particle size after attachment of PEG 5,000 is slightly greater than 100 nm (7590, col. 2), table); it is deemed inherent that without PEG the particle size is less than 100 nm. Neradovic also

suggests that these micelles are useful as drug delivery systems (7589, col. 1, 7591, paragraphs bridging col. 1 and 2).

Neradovic does not specifically disclose the micelles in conjunction with a drug (a controlled release system; a targeting drug composition).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use the micelles of Neradovic to deliver drugs. The motivation is to follow the explicit suggestion of the prior art. Since Neradovic specifically suggests this manipulation, the artisan would enjoy a reasonable expectation of success.

Claims 1-7 and 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neradovic et al (*Macromolecules*, 2001) in view of US 5,939,453 ('453). The relevant portions of Neradovic are given above.

Neradovic et al fails to teach an ABA block copolymer. Neradovic et al further fails to teach adding a homing device.

'453 teaches that AB and ABA block copolymers are equivalents in the art of forming polymer micelles (abstract). Heller further teaches such micelles may be suspended in oils such as corn oil, cottonseed oil, peanut oil and sesame oil as adjuvants for drug delivery (col 13, lines 47-55).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to prepare the polymer of Neradovic as an ABA triblock copolymer rather than as an AB diblock. The motivation is that he two types of polymer

architectures are recognized as equivalent in the art, and as such are considered to be obvious variants. Therefore the artisan would enjoy a reasonable expectation of success at making the ABA copolymer, and would expect the ABA copolymer to have similar properties to the AB copolymer of the art. It would have been further obvious to add an adjuvant, such as corn oil, for drug delivery. Corn oil is a homing device for corn oil. The motivation for adding an adjuvant such as corn oil is because it is an art recognized medium in which polymer micelles may be suspended for drug delivery.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

December 3, 2010